

What is claimed is:

1. A method for generating phosphorothioate oligo mixtures comprising:
 - 1) growing a single-stranded recombinant DNA phage in modified media that uses thio-phosphate as a source of phosphate
 - 2) harvesting the single-stranded phage and purifying the DNA corresponding to the recombinant DNA insert
 - 3) fragmentation of the insert DNA such that oligo mixtures spanning the entire length of the segment are generated.
2. The method of claim 1 used to generate phosphorothioate ds DNA, ss DNA, and/or RNA by in vivo incorporation of thio-phosphate into nucleotide precursor pools.
3. The method of claim 1 used to generate ds DNA, ss DNA, or RNA partially substituted with phosphorothioate linkages by culturing cells in media consisting of a mixture of thio-phosphate and inorganic phosphate.
4. The method of claim 1 wherein the cells cultured in thio-phosphate media or induced to uptake thio-phosphate are of prokaryotic or eukaryotic origin.
5. The method of claim 1 using other derivatives of phosphate such as those substituted with one or more sulfur group, methyl group or other moiety.